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Editorial

EDITORIAL

Toward Using Breast Cancer Risk Prediction Models for Guiding Screening Decisions

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Although screening recommendations for average-risk women tend to be based solely on sex and age, in recent years investigators have been exploring more complex personalized screening strategies with the goal of tailoring recommendations for age to start, screening intervals, and screening protocols to an individual's estimated risk. Risk estimates are often obtained from models predicting the absolute risk of breast cancer. Several widely known breast cancer risk prediction models exist (1), although utilization is mostly in high-risk populations because there is little guidance for how these models can be used to modify current screening guidelines for average-risk women.

In this issue of the Journal, Kerlikowske and colleagues (2) present a new breast cancer risk prediction model. The model is developed and validated using data on women in the Breast Cancer Surveillance Consortium (BCSC) who were undergoing approximately annual or biennial mammography with data captured by participating mammography registries. The model uses information on a woman's race and ethnicity, current age, body mass index, menopausal status, breast density, family history of breast cancer, and findings from prior breast biopsies.

How is this model different from all other breast cancer prediction models? First, in contrast to other models that tend to model the risk of all invasive breast cancer, this one models the risk of advanced invasive breast cancer, the premise being that these are the aggressively growing tumors that are critical to catch quickly so that less intensive treatment might be used and mortality reduced. Second, Kerlikowske and colleagues (2) focus on modeling breast cancer risk within a short time interval after a screening exam: 12 months for annual screeners (defined as having a mammogram 11-18 months beforehand allowing for variation in when women schedule exams) and 24 months for biennial screeners (who had prior mammograms within 19-30 months). This risk is then accumulated up to either 6 or 3 rounds of screening (for annual and biennial screeners, respectively) to present the 6-year cumulative risk. In comparison, in other models, the timing of screening exams is not a central component of the modeling process and usually is not considered.

These key differences move breast cancer risk prediction modeling in an important direction. With their approach, Kerlikowske et al. (2) aim to facilitate the usefulness of their model when making screening decisions, at both the individual patient level and the population level when formulating screening guidelines.

Before this model is adopted into widespread practice, though, it should be evaluated in other data (3). With more than 900 000 women from multiple sites across the United States contributing to the current analysis, the BCSC is a unique, rich resource that is not easily replicated. Although BCSC demographics may be similar to the US population, most of the United States is not covered by a BCSC registry. We do not know if the model will perform similarly for women with mammograms performed outside of the registries' catchment areas and interpreted by radiologists who are not at one of the BCSC-contributing facilities. Validating the model using data from diverse sites and populations across the United States is essential. In the absence of existing high-quality databases that can be used for this purpose, a necessary first step is the collection of the relevant data components from medical records and radiology databases in a systematic fashion.

Motivating the work by Kerlikowske et al. (2) is the desire to differentiate patients who are at high risk of advanced cancer and should be screened annually vs patients at lower risk who would achieve the same benefit from biennial screening. A main argument in favor of biennial screening is the reduction in the harms of screening (ie, recall and downstream testing) associated with more frequent screening encounters. Although fewer encounters with mammography screening is one approach to harm reduction, we should not neglect the importance of improving the accuracy of mammography, through either advances in technology or improved reader performance. Indeed, digital breast tomosynthesis, representing just 5% of the examinations in the current analysis, has been reported to have improved specificity compared with 2D digital mammography alone (4,5) and may reduce these harms. It will be

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interesting to see if increasing uptake of digital breast tomosynthesis changes outcomes.

Using the model at an individual level to guide recommendations to patients or as a vehicle for shared decision making will require that physicians incorporate it into clinical care. Risk estimates will need to be updated regularly. The online risk calculator that Kerlikowske and colleagues are developing will help with this task, especially if it can be integrated into electronic health records. However, previous studies have pointed out barriers to using statistical risk estimates in clinical care, including time pressures faced by physicians and the ability of physicians and patients to discuss and understand risk estimates (6–8). Patients must also be willing to adhere to recommendations, and as the authors note, this study does not address individual preferences and whether these would align with model predictions.

In some respects, this model mirrors real-world experience in the United States. Although leading organizations recommend an annual, biennial, or hybrid model of age-specific screening intervals, most women do not perfectly adhere to the specific interval they or their provider intend. The model aims to estimate the risk of being diagnosed with an advanced breast cancer as a function of personal risk; however, a woman whose next screening exam occurred 30 months after the last one may have been diagnosed with an advanced breast cancer simply because too much time elapsed after her previous normal exam. The model relies primarily on biological factors that influence the risk of being diagnosed with advanced breast cancer. However, evidence also shows that the quality of screening and regular adherence to recommended screening intervals are also factors in reducing risk of an advanced breast cancer (9,10).

Finally, the conclusive test of whether a risk prediction model works well involves evaluating how it affects health outcomes. Will following the recommended screening strategy reduce overdiagnosis and unnecessary recalls? Will the model's direction for risk-based screening avert more premature deaths from breast cancer? Ongoing evaluation in a large representative population is important to address these questions.

The goal of personalized risk-based screening has been elusive, but the BCSC authors have proposed a novel approach that takes us closer to that goal. Most states have breast cancer density notification requirements, but a system of guideline-recommended care with insurance coverage of recommended screening protocols, especially for high-risk women, should become a priority. Much work remains, including taking the steps to ensure that health records include data necessary to apply this model. Let us hope that the resources and determination to achieve this goal will support moving forward.

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